

**Amendments to the Claims**

*New Claims*

The listing of claims will replace all prior versions, and listings, of claims in the application:

**Claim Listing**

1. (Currently amended) A method for enhancing the effect of a vaccine, the method comprising administering to a patient in need thereof, a vaccine pharmaceutical composition comprising pharmaceutically acceptable particles, the particles comprising
  - (i) a biologically active agent that generates a protective immune response in an animal to which it is administered; in combination with
  - (ii) a first adjuvant chemical which increases the effect of the biologically active agent, said adjuvant chemical selected from one or more being selected from the group consisting of:
    - A) polyornithine,
    - B) a water soluble vitamin or water soluble vitamin derivative,
    - C) a positively charged cationic block copolymer or a positively charged cationic surfactant,
    - D) a clathrate,
    - E) a complexing agent,
    - F) cetrimides,
    - G) an S-layer protein, or
    - H) Methyl-glucamine; and
  - (iii) a pharmaceutically acceptable carrier or diluent; subject to the following provisos
    - a) when the chemical (ii) above is selected from D) or E), the biologically active agent is an agent that generates a protective immune response in an animal to which it is administered;
    - b) when the adjuvant chemical (ii) above is selected from A) and the biologically active agent is an agent that generates a protective immune

**Second Amendment and Response to Office Action**

**Serial No. 09/937,068**

**Page 3 of 8**

~~response in an animal to which it is administered, the composition is for administration to a mucosal surface,~~

~~e) b) when the adjuvant chemical (ii) above is selected from C) and the biologically active agent is an agent that generates a protective immune response in an animal to which it is administered, the composition does not contain a polyacrylic acid, and~~

~~d) c) when the adjuvant chemical (ii) above is selected from G) and the biologically active agent is an agent that generates a protective immune response in an animal to which it is administered, the carrier or diluent of (iii) particle is a microsphere or liposome.~~

**Claim 2 (Cancelled)**

3. (Currently amended) The ~~composition method~~ of claim 1 wherein the adjuvant chemical acts as an immunostimulant.

4. (Currently amended) The ~~composition method~~ of claim 1 wherein the said adjuvant chemical is selected from one or more of;

A) ~~the polyornithine polyornithine has having~~ a molecular weight from 5 to 150kDa;

B) ~~the water soluble vitamin or water soluble vitamin derivative is vitamin E TPGS (d-alpha tocophenyl polyethylene glycol 1000 succinate),~~

C) ~~the a cationic block copolymer or the a cationic surfactant, is positively charged by means of NH<sub>2</sub><sup>+</sup> groups~~

D) ~~the a complexing agent that forms complexes with fatty acids, or~~

E) ~~the clathrate is a cyclodextrin or a derivative thereof.~~

5. (Cancelled)

**Second Amendment and Response to Office Action**

**Serial No. 09/937,068**

**Page 4 of 8**

6. (Currently amended) The composition method of claim 5 1 wherein the particle is a microsphere or liposome particles are microspheres or liposomes.

7. (Currently amended) The composition method of claim 6 which comprises a microsphere wherein the particles are microspheres.

8. (Currently amended) The composition method of claim 7 wherein the microsphere is microspheres are prepared using a high molecular weight polymer.

9. (Currently amended) The composition method of claim 8 wherein the polymer has a molecular weight of 100kDa or more.

10. (Currently amended) The composition method of claim 7 wherein the microsphere comprises poly-(L-lactide).

Claim 11 (Cancelled)

12. (Currently amended) The composition method of claim 1 which wherein the vaccine composition is administered to a mucosal surface of the animal or administered parenterally to the animal.

13. (Currently amended) The composition method of claim 1 2 which wherein the vaccine composition further comprises a second adjuvant.

Claims 14-25 (Withdrawn)

26. (Currently amended) The composition method of claim 4 30 wherein  
A) the complexing agent forms complexes with deoxycholic acid; or  
B) the clathrate is dimethyl- $\beta$ -cyclodextrin .

***Second Amendment and Response to Office Action***

**Serial No. 09/937,068**

**Page 5 of 8**

27. (New) The method of claim 1 wherein the adjuvant chemical is A) polyornithine having a molecular weight from 5 to 150 kDa.

28 (New) The method of claim 1 wherein the adjuvant chemical is B) a water soluble vitamin or water soluble vitamin derivative comprising vitamin E TPGS (d-alpha tocophenyl polyethylene glycol 1000 succinate).

29. (New) The method of claim 1 wherein the adjuvant chemical is C) a cationic block copolymer or a cationic surfactant, positively charged by means of  $\text{NH}_2^+$  groups.

30. (New) The method of claim 1 wherein the adjuvant chemical is E) a complexing agent that forms complexes with fatty acids.

# *Old Claims*

## Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of the claims in the application.

### Listing of Claims

1. (Currently amended) A pharmaceutical composition comprising
  - (i) a biologically active agent;
  - (ii) ~~an a first~~ adjuvant chemical which increases the effect of the biologically active agent, said chemical selected from one or more of:
    - A) ~~a polyamino acid polyornithine,~~
    - B) a water soluble vitamin or ~~water soluble~~ vitamin derivative,
    - C) ~~a positively charged cationic pluronics block copolymer or a positively charged cationic surfactant,~~
    - D) a clathrate,
    - E) a complexing agent,
    - F) cetrimides,
    - G) an S-layer protein, or
    - H) Methyl-glucamine; and
  - (iii) a pharmaceutically acceptable carrier or diluent; subject to the following provisos

- a) when the chemical (ii) above is selected from D) or E), the biologically active agent is an agent ~~which is capable of generating~~ that generates a protective immune response in an animal to which it is administered;
- b) when the chemical (ii) above is selected from A) and the biologically active agent is an agent ~~which is capable of generating~~ that generates a protective immune response in an animal to which it is administered, the composition is for administration to a mucosal surface,
- c) when the chemical (ii) above is selected from C) and the biologically active agent is an agent ~~which is capable of generating~~ that generates a protective immune response in an animal to which it is administered, the composition does not contain a polyacrylic acid, and
- d) when the chemical (ii) above is selected from G) and the biologically active agent is an agent ~~which is capable of generating~~ that generates a protective immune response in an animal to which it is administered, the carrier or diluent of (iii) is a microsphere or liposome.

2. (Currently amended) ~~A~~ The composition ~~according to~~ of claim 1 wherein the biologically active agent is an agent ~~that is capable of generating~~ generates a protective immune response in an animal to which it is administered.

3. (Currently amended) A The composition according to of claim 1  
wherein the said adjuvant chemical ~~can act~~ acts as an immunostimulant.

4. (Currently amended) A The composition according to of claim 1  
wherein the said adjuvant chemical is selected from one or more of;

- A) the poly-ornithine has a, for example of molecular weight from 5 to 150kDa;
- B) the water soluble vitamin vitamins or water soluble vitamin derivative derivatives is such as vitamin E TPGS (d-alpha tocophenyl polyethylene glycol 1000 succinate),
- C) the cationic pluronics which are block copolymer copolymers or the cationic surfactant is surfactants which are positively charged by means of, in particular with NH<sub>2</sub><sup>+</sup> groups
- D) the complexing agent forms agents which form complexes with fatty acids such as deoxycholic acid, or
- E) the clathrate is a cyclodextrin or a derivative thereof cyclodextrins and their derivatives such as dimethyl β cyclodextrin.

5. (Currently amended) A The composition according to of claim 1  
wherein the carrier comprises a particle.

6. (Currently amended) A The composition ~~according to~~ of claim 5  
wherein the particle is a microsphere or liposome.

7. (Currently amended) A The composition ~~according to~~ of claim 6 which  
comprises a microsphere.

8. (Currently amended) A The composition ~~according to~~ of claim 7  
wherein the microsphere is prepared using a high molecular weight polymer.

9. (Currently amended) A The composition ~~according to~~ of claim 8  
wherein the polymer has a molecular weight of 100kDa or more.

10. (Currently amended) A The composition ~~according to~~ of claim 7  
wherein the microsphere comprises poly-(L-lactide).

11. (Currently amended) A The composition ~~according to~~ of claim 1  
wherein the ratio of the chemical (ii) to the carrier (iii) is from 99:1 to 9:1 w/w.

12. (Currently amended) A The composition ~~according to~~ of claim 1 which  
~~is adapted for administration to a mucosal surface or is suitable for parenteral administration~~  
administered to a mucosal surface of the animal or administered parenterally to the animal.

13. (Currently amended) A The composition according to of claim 2 which further comprises a furthersecond adjuvant.

14. (Withdrawn) A method of producing a prophylactic or therapeutic vaccine, which method comprises encapsulating a polypeptide which is capable of producing a protective immune response in a first polymeric material which has a high molecular weight, in the presence of a second polymeric material which increases the biological effect of the composition.

15. (Withdrawn) A method of protecting a mammal against infection, which method comprises administration of a composition according to claim 1 to a mammal.

16. (Withdrawn) A method according to claim 15 wherein the composition is applied to a mucosal surface.

17. (Withdrawn) A method according to claim 16 wherein the mucosal surface comprises an intranasal surface.

18. (Withdrawn) A microsphere comprising a polymeric carrier and an S-layer protein.

19. (Withdrawn) A microsphere according to claim 18 wherein said S-layer protein is coated on the surface of the microsphere.

20. (Withdrawn) A microsphere according to claim 18 which further comprises an agent that is capable of generating a protective immune response in an animal to which it is administered.

21. (Withdrawn) A microsphere according to claim 20 wherein one or more of said agents are linked to the S-layer protein.

22. (Withdrawn) A pharmaceutical composition comprising a microsphere according to claim 19.

23. (Withdrawn) A pharmaceutical composition according to claim 22 wherein said composition is a vaccine, intended to produce a protective immune response against a bacterium, and said S-layer protein is derived from said bacterium.

24. (Withdrawn) The use of a chemical selected from  
A) a polyamino acid,  
B) a water soluble vitamin or vitamin derivative,

- C) positively charged cationic pluronics,
- D) a clathrate,
- E) a complexing agent,
- F) cetrimides,
- G) an S-layer protein, or
- H) Methyl-glucamine

as an immunostimulant, provided that in the case of A), the immunostimulant is applied to a mucosal surface, in the case of C, the compound is used in the absence of a polyacrylic acid.

25. (Withdrawn) The use of an adjuvant chemical selected from

- A) a polyamino acid,
- B) a water soluble vitamin or vitamin derivative,
- C) positively charged cationic pluronics,
- D) a clathrate,
- E) a complexing agent,
- F) cetrimides,
- G) an S-layer protein, or
- H) Methyl-glucamine

as an immunostimulant in the production of a vaccine for use in prophylactic or therapeutic treatment, provided that in the case of A), the immunostimulant is used in a vaccine which is

applied to a mucosal surface, in the case of C), the compound is used in the absence of a polyacrylic acid.

26. (New) The composition of claim 4 wherein
- A) the complexing agent forms complexes with deoxycholic acid; or
  - B) the clathrate is dimethyl- $\beta$ -cyclodextrin.